Case 9

2015-11-12
67 y ♂

Supraumbilical tumor in an old scar
Indikationen Sentinel Lymphknoten
## Your Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Nodular basal cell carcinoma (BCC)</td>
<td>20%</td>
</tr>
<tr>
<td>2 Nodulocystic BCC</td>
<td></td>
</tr>
<tr>
<td>1 Adenoid BCC/keratotic BCC</td>
<td></td>
</tr>
<tr>
<td>11 BCC, NOS</td>
<td>54%</td>
</tr>
<tr>
<td>2 Solid BCC</td>
<td></td>
</tr>
<tr>
<td>4 Trichoblastoma/2 Trichoepithelioma</td>
<td></td>
</tr>
<tr>
<td>3 BCC with trichogenic differentiation</td>
<td></td>
</tr>
<tr>
<td>2 Metastasis of GI-Carcinoma</td>
<td>26%</td>
</tr>
<tr>
<td>2 Merkel cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>1 Cutaneous NET</td>
<td></td>
</tr>
<tr>
<td>1 Basosquamous carcinoma</td>
<td></td>
</tr>
<tr>
<td>1 Malignant adnex tumor/basaloid tumor/follicular diff./trichilemmal adnex tumor/spiradenoma</td>
<td></td>
</tr>
</tbody>
</table>
Diagnosis:
Nodular basal cell carcinoma
BCC: Most common subtypes

- Superficial
- Nodular (various subtypes)
- Micronodular
- Infiltrative (non) sclerodermiform

Basaloid skin tumours: Basal cell carcinoma.
*Current Diagnostic Pathology 2007; 13:252-272*
Carr RA et al.
Nodular BCC
DD: Trichoblastoma

Benign, biphasic epithelial-mesenchymal neoplasm with various growth patterns:
Large nodular, small nodular, retiform, cribriform, racemiform, adamantinoid

DD: Trichoepithelioma, nodular BCC

Papillary mesenchymal body

germ
papilla
DD: Trichoeplitlioma

Trichoeplitlioma:
«Superficial trichoblastoma» with prominent superficial follicular differentiation
DD: Trichoblastoma, nodular BCC

Bulb & papilla
CD10
DD: Desmoplastic Trichoepithelioma

<table>
<thead>
<tr>
<th>Morpheeic BCC</th>
<th>DesmoTricho</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ki67&gt;10%</td>
<td>Ki67&lt;10%</td>
</tr>
<tr>
<td>bcl-2 diffuse</td>
<td>bcl-2 peripheral</td>
</tr>
<tr>
<td>BerEP4 diffuse</td>
<td>BerEP4 focal</td>
</tr>
<tr>
<td>No Merkel cells</td>
<td>CK20+ Merkel cells</td>
</tr>
</tbody>
</table>

Central depression
Superficial BCC

More commonly involving the trunk.
Higher rate of incomplete excision and local recurrence.
Do not involve the reticular dermis. No more than 1mm in thickness.
Micronodular BCC

<25 cells/nodule, <0.15mm
More local recurrence
Penetrate more deeply
Less retraction artefact
Less palisading
Frequent Pn1
Infiltrative (Non-) Sclerodermiform

Infiltrative non-sclerodermiform →

Infiltrative sclerodermiform ↓
## Risk Stratification in BCC

### Clinical Risk Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size and location</td>
<td></td>
</tr>
<tr>
<td>Trunk, extremities</td>
<td>≥ 20 mm</td>
</tr>
<tr>
<td>Cheeks, forehead, neck, scalp</td>
<td>≥ 10 mm</td>
</tr>
<tr>
<td>Mask area, genitalia, hands, feet</td>
<td>≥ 6 mm</td>
</tr>
<tr>
<td>Borders</td>
<td>poorly defined</td>
</tr>
<tr>
<td>Primary vs. recurrent</td>
<td>Recurrent</td>
</tr>
<tr>
<td>Site of prior radiation</td>
<td>yes</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>yes</td>
</tr>
</tbody>
</table>

### Pathologic Risk Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perineural involvement</td>
<td>yes</td>
</tr>
<tr>
<td>Histopathologic subtypes</td>
<td>micronodular, infiltrative, sclerodermiform</td>
</tr>
</tbody>
</table>

A single high-risk factor places the patient in a high-risk category.

*Am J Dermatopathol*  
2012; 34(7): 737-745
## Surgical Margins

<table>
<thead>
<tr>
<th>Recommendations for Clinical Margins</th>
<th>Low-risk</th>
<th>High-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>4 mm margin of normal appearing skin</td>
<td>Mohs Surgery (0-11% recurrences) or resection with complete circumferential peripheral and deep margin assessment</td>
</tr>
</tbody>
</table>

*Am J Dermatopathol*

2012; 34(7): 737-745
Histologic Variants of BCC

- Adamantinoid
- Apocrine
- Basosquamous (metatypical)
- Cicatrical, keloidal
- Clear cell
- Eccrine
- Fibroepithelioma of Pinkus
- Follicular
- Giant Cell
- Granular cell
- Infundibulocystic
- Matrical
- Myoepithelial
- Neuroendocrine differentiation
- Sebaceous
- Signet ring/hyaline inclusion
- Tricholemmal
Collision tumors: BCC and SCC as separate tumors (a)
Metatypical BCC (b) and basosquamous BCC
Small foci of keratinization within BCC (c)
SCC with basaloid peripheries vs. BCC with keratotic differentiation
BCC with pseudoepitheliomatous hyperplasia
Bowenoid actinic keratosis imitating superficial BCC
Pseudoepitheliomatosus Hyperplasia

Basal cell carcinoma-associated paratumoral follicular and epidermal hyperplasia.

Actinic keratosis vs. superficial BCC in superficial biopsies:

1. Step sections
2. IHC:
   Ber-EP4 (BCC +, bowenoid epidermal dysplasia (+))
   EMA (SCC +, AK +)
BCC with Ductal Differentiation

Basal cell carcinoma with unusual Histologic patterns.

Basal cell carcinoma with ductal and glandular differentiation.
*Eur J Dermatol* 2004; 14:383-387
Adenoid BCC
Clear Cell BCC
Boweonid BCC

Variant usually of nodular tumors. Prominent cellular atypia, necroses, atypical mitoses.

Present clinically as typical BCC and behave as ordinary BCC.
Metastasizing BCC

**Risk factors:**
- Sun exposed area (head & neck)
- Large (>10 cm²)
- Multiple primary BCC
- Long-standing lesion
- Perineural invasion
- Histology: basosquamous, metatypical, sclerodermiform

**Frequency of metastases:**
- Lymph nodes 40-83%
- Lungs 35-53%
- Bones 20-28%
- Skin 10-17%
- Liver 9%

Normal Sonic Hedgehog Pathway

Embryo: active Hedgehog signaling

Normal adult: HH signaling repressed by patched

Seminars in Oncology 2012; 39(2):139-144
Hautarzt 2010; 61:356-358
Sonic Hedgehog Pathway in BCC

BCC: reactivation of HH signaling

targeted therapy: selective inhibition of HH signaling

HH

PTCH1

SMO

Gli

Gli target genes active

Gli target genes inactive

67-90% inactivating somatic or germline mutations or loss (Gorlin Goltz)

10-20% Somatic activating mutations → Resistance to PTCH1 inactivation

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What are your questions?